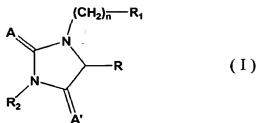


WHAT IS CLAIMED IS:

1. A compound having the Formula I:



or a pharmaceutically acceptable salt, or solvate thereof, wherein:

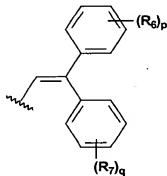
n is 0 to 3;

A and A' are independently oxygen or sulfur;

R is hydrogen, linear or branched alkyl, benzyl, hydroxybenzyl, thioalkyl, alkylthioalkyl, hydroxyalkyl, aminoalkyl, guanidinyllalkyl, carboxyalkyl or aminocarboxyalkyl;

R₁ is selected from the group consisting of:

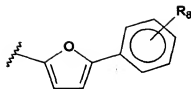
- (i) optionally substituted phenoxyphenyl;
- (ii) optionally substituted benzyloxyphenyl;
- (iii) optionally substituted phenylthiophenyl;
- (iv) optionally substituted benzylthiophenyl;
- (v) optionally substituted phenylaminophenyl;
- (vi) optionally substituted benzylaminophenyl; and
- (vii)



wherein each occurrence of R₆ and each occurrence of R₇ are independently hydrogen or alkyl; and

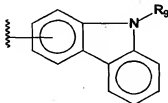
p and q are independently integers from zero to 4;

(viii)



wherein R₈ is hydrogen, halogen, hydroxy, C₁₋₆ alkyl, C₁₋₆ alkoxy, cyano, amino, or nitro;

(ix)



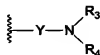
wherein R₉ is hydrogen or C₁₋₆ alkyl; and

(x) optionally substituted naphthdyl;

and

R₂ is selected from the group consisting of:

(i)



where

Y is an optionally substituted C₂₋₆ alkylene, and

R₃ and R₄ are the same or different and are hydrogen, alkyl, or aryl, or R₃ and R₄ together form an alkylene chain having 3 to 5 carbon atoms, optionally substituted with an alkyl or aryl moiety, or said alkylene chain is optionally interrupted by an oxygen atom or -NR₅, where R₅ is hydrogen or C₁₋₆ alkyl;

(ii) pyridylalkyl; and

(iii) piperidin-4-ylalkyl, optionally substituted by alkyl, aryl or alkyl.

2. The compound according to claim 1, wherein R₂ is -YNR₃R₄, and an optionally substituted C₂₋₆ alkylene.

3. The compound according to claim 2, wherein:

R_1 is optionally substituted phenoxyphenyl or optionally substituted benzyloxyphenyl; R_3 and R_4 together form an alkylene chain having 4 to 5 carbon atoms; and Y is an optionally substituted C_{2-4} alkylene chain.

4. The compound according to claim 3, wherein R_3 and R_4 together form an alkylene chain of 5 carbon atoms; and Y is an optionally substituted C_{2-4} alkylene chain.

5. The compound according to claim 3, wherein R_3 and R_4 together form an alkylene chain of 4 carbon atoms, and Y is an optionally substituted C_{2-4} alkylene chain.

6. The compound according to claim 2, wherein Y is ethylene or propylene.

7. The compound according to claim 2, wherein:

R_1 is optionally substituted phenoxyphenyl or optionally substituted benzyloxyphenyl; R_3 and R_4 are independently hydrogen, alkyl or aryl; and Y is an optionally substituted C_{2-4} alkylene chain.

8. The compound according to claim 1, wherein n is 1.

9. The compound according to claim 1, wherein n is 0.

10. The compound according to claim 1, wherein R_1 is an optionally substituted phenoxyphenyl.

11. The compound according to claim 1, wherein R_1 is an optionally substituted benzyloxyphenyl.

12. The compound according to claim 1, wherein $-(CH_2)_n-$ is attached to the 3- or 4-position of the phenyl component of the phenoxyphenyl or the benzyloxyphenyl defined by R_1 .

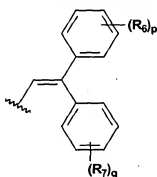
13. The compound according to claim 10, wherein n is 1; R_2 is $-YNR_3R_4$, Y is C_{2-6} alkylene; and R_3 and R_4 together form an alkylene chain having 4 to 5 carbon atoms.

14. The compound according to claim 11, wherein n is 1; R_2 is $-YNR_3R_4$, Y is C_{2-6} alkylene; and R_3 and R_4 together form an alkylene chain having 4 to 5 carbon atoms.

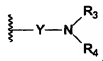
15. The compound according to claim 10, wherein n is 1; R_2 is $-YNR_3R_4$, Y is C_{2-6} alkylene; and R_3 and R_4 are the same or different and are selected from hydrogen, alkyl, or aryl.

16. The compound according to claim 11, wherein n is 1; R_2 is $-YNR_3R_4$, Y is C_{2-6} alkylene; and R_3 and R_4 are the same or different and are selected from hydrogen, alkyl, or aryl.

17. The compound according to claim 1, wherein R_1 is



18. The compound according to claim 17, wherein R_2 is

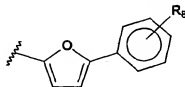


19. The compound according to claim 17 wherein Y is a C₂₋₆ alkylene, and R₃ and R₄ are the same or different and are selected from hydrogen, alkyl, or aryl.

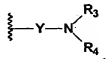
20. The compound according to claim 18, wherein Y is a C₂₋₆ alkylene, and, R₃ and R₄ together form an alkylene chain having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.

21. The compound according to claim 20, wherein said alkylene chain formed from taking R₃ and R₄ together is further interrupted by an oxygen atom or -NR₅, where R₅ is hydrogen or C₁₋₆ alkyl.

22. The compound according to claim 1, wherein R₁ is



23. The compound according to claim 22, wherein R₂ is

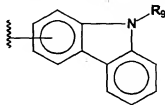


24. The compound according to claim 23, wherein Y is a C₂₋₆ alkylene, and R₃ and R₄ are the same or different and are selected from hydrogen, alkyl, or aryl.

25. The compound according to claim 23, wherein Y is a C₂₋₆ alkylene, and, R₃ and R₄ together form an alkylene chain having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.

26. The compound according to claim 25, wherein said alkylene chain formed from taking R₃ and R₄ together is further interrupted by an oxygen atom or -NR₅, where R₅ is hydrogen or alkyl.

27. The compound according to claim 1, wherein R_1 is



28. The compound according to claim 27, wherein R_2 is



29. The compound according to claim 28, wherein Y is a C_{2-6} alkylene, and R_3 and R_4 are the same or different and are selected from hydrogen, alkyl, or aryl.

30. The compound according to claim 28, wherein Y is a C_{2-6} alkylene, and, R_3 and R_4 together form an alkylene chain having 4 to 5 carbon atoms, optionally substituted with an alkyl or aryl moiety.

31. The compound according to claim 30, wherein said alkylene chain formed from taking R_3 and R_4 together is further interrupted by an oxygen atom or $-NR_5$, where R_5 is hydrogen or alkyl.

32. The compound according to claim 1, wherein R_1 is naphthyl.

33. The compound according to claim 31, wherein R_2 is



34. The compound according to claim 32, wherein Y is a C₂₋₆ alkylene, and R₃ and R₄ are the same or different and are selected from hydrogen, alkyl, or aryl.
35. The compound according to claim 33, wherein Y is a C₂₋₆ alkylene, and, R₃ and R₄ together form an alkylene chain having 4 to 5 carbon atoms, which is optionally substituted with an alkyl or aryl moiety.
36. The compound according to claim 35, wherein said alkylene chain is further interrupted by an oxygen atom or -NR₅, where R₅ is hydrogen or alkyl.
37. The compound according to claim 1, wherein said compound is selected from the group consisting of:
- 3-(2-piperidinylethyl)-1-(4-(4-fluorophenoxy)benzyl) hydantoin;
 - 3-(2-piperidinylethyl)-1-(4-(benzyloxy)benzyl) hydantoin;
 - 3-(2-piperidinylethyl)-1-(3-(4-trifluoromethylphenoxy)benzyl) hydantoin;
 - 3-(2-piperidinylethyl)-1-(3-(3,4-dichlorophenoxy)benzyl) hydantoin;
 - 3-(2-piperidinylethyl)-1-(3-(phenoxy)benzyl) hydantoin; and
 - 3-(2-piperidinylethyl)-1-(3-(benzyloxy)benzyl) hydantoin.
38. A pharmaceutical composition, comprising the compound of claim 1, and a pharmaceutically acceptable carrier or diluent.
39. A method of making a compound according to claim 1 wherein said method comprises:
- (a) reacting an amine-protected amino acid with a resin-supported hydroxy group to produce a resin-supported, amine-protected, amino acid;
 - (b) deprotecting said resin-supported amine-protected amino acid, to produce a resin-supported amino acid having an N-terminus primary amine;
 - (c) reacting said resin-supported amino acid obtained in step (b), with an aldehyde to produce a resin-supported enamine;

(d) reducing said resin-supported enamine obtained in from step (c), to produce a resin-supported amino acid, having an N-terminus secondary amine;

(e) reacting said resin-supported amino acid obtained from step (d), with triphosgene, to produce a resin-supported amino acid having an N-terminus tertiary amine, wherein said tertiary amine comprises a carbonyl chloride moiety;

(f) reacting said resin-supported amino acid obtained from step (e), with a primary amine; and

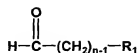
(g) releasing a product obtained from step (f) from its support, to obtain the compound of Formula I.

40. The method according to claim 39, wherein said resin is a Wang resin.

41. The method according to claim 39, wherein step (a) is carried out in the presence of DMF, DIC and DMAP.

42. The method according to claim 39, wherein step (b) is carried out in the presence of piperidine and DMF.

43. The method according to claim 39, wherein said aldehyde of step (c) has the formula:



wherein:

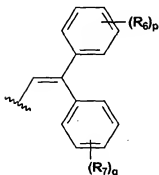
n is an integer from 1-3; and

R₁ is selected from the group consisting of:

- (i) optionally substituted phenoxyphenyl;
- (ii) optionally substituted benzyloxyphenyl;
- (iii) optionally substituted phenylthiophenyl;
- (iv) optionally substituted benzylthiophenyl;
- (v) optionally substituted phenylaminophenyl;

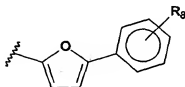
(vi) optionally substituted benzylaminophenyl;

(vii)



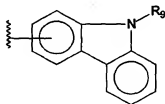
wherein R_6 and R_7 are independently hydrogen or alkyl; and p and q are independently integers from 0 to 4;

(viii)



wherein R_8 is hydrogen or alkyl;

(ix)

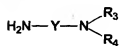


wherein R_9 is hydrogen or alkyl; and

(x) naphthyl.

44. The method according to claim 39, wherein said primary amine of step (f) is selected from the group consisting of:

(i) an amine of the formula:



wherein

Y is an optionally substituted C_{2-6} alkylene; and

R₃ and R₄ are the same or different and are selected from hydrogen, alkyl, or aryl, or R₃ and R₄ together form an alkylene chain having 4 to 5 carbon atoms, optionally substituted with an alkyl or aryl moiety, and said alkylene chain is optionally interrupted by an oxygen atom or -NR₅, where R₅ is hydrogen or alkyl;

- (ii) pyridylalkyl amine; and
- (iii) an optionally substituted piperidin-4-ylalkyl amine, wherein optional substituents are selected from the group consisting of alkyl, aryl or aralkyl.

45. The method according to claim 44, wherein said primary amine is 1-(2-aminoethyl)piperidine; (2-aminoethyl)pyrrolidine; or di(2-propyl)(2-aminoethyl) amine.

46. The method according to claim 39, wherein step (e) is carried out in the presence of DMF and pyridine.

47. A method of treating, preventing or ameliorating a disorder responsive to blockage of sodium channels in a mammal, comprising administering to a mammal in need thereof an effective amount of a compound according to claim 1, or pharmaceutically acceptable salt thereof.

48. The method according to claim 47, wherein said disorder is selected from the group consisting of: neuronal damage; a neurodegenerative condition, acute or chronic pain, depression, and diabetic neuropathy.

49. The method according to claim 47, wherein said neuronal damage is caused by focal or global ischemia.

50. The method according to claim 47, wherein said neurodegenerative condition is amyotrophic lateral sclerosis (ALS).

51. The compound according to claim 1, wherein said compound functions as an antitinnitus agent, anticonvulsant, antiarrhythmic, local anesthetic, or antimanic depressant.

52. A method of treating a mammal suffering from a disorder responsive to blockage of sodium channels, said method comprising administering to said mammal a compound according to claim 1, or pharmaceutically acceptable salt thereof, in an amount that is effective for treating said disorder.

53. The method according to claim 52 wherein said mammal is a human, dog or cat.

54. The method according to claim 53, wherein said disorder is selected from the group consisting of: neuronal damage; a neurodegenerative condition, acute or chronic pain, depression, and diabetic neuropathy.

55. The method according to claim 53, wherein said neuronal damage is caused by focal or global ischemia.

56. The method according to claim 53, wherein said neurodegenerative condition is amyotrophic lateral sclerosis (ALS).

57. The compound according to claim 37, wherein the compound is selected from the group consisting of:

3-(2-piperidinylethyl)-1-(3-(4-trifluoromethylphenoxy)benzyl)

hydantoin;

3-(2-piperidinylethyl)-1-(3-(3,4-dichlorophenoxy)benzyl)hydantoin;

and

3-(2-piperidinylethyl)-1-(3-(benzyloxy)benzyl)hydantoin.